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**Chromatin looping is needed for iPSC induction.**

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**Authors:** Ji-Fan Hu, Andrew R Hoffman

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**Public Summary:**

Somatic cells can be reset to pluripotent capability by ectopic expression of defined factors to form so-called "induced pluripotent stem cells" (iPSCs). Although it is now routine to reprogram somatic cells into iPSCs, the process is extremely inefficient, preventing the immediate translation of this promising technology into clinics. Using chromatin immunoprecipitation assay (ChIP), we found that defined factors, in spite of binding to their target promoters, failed to induce transcription from these genes, suggesting that the activation of endogenous pluripotency genes may represent a critical reprogramming block preventing iPSC induction. Using chromosome conformation capture (3C), we found that the formation of intrachromosomal looping in pluripotency-associated genes constituted a critical epigenetic barrier that must be overcome for activation of pluripotency-associated genes. Taken together, it is clear that the requirement for chromatin loops between the enhancers and promoters of certain pluripotency genes is a critical epigenetic barrier that must be overcome for a cell to be transformed to pluripotency. It will be important to identify endogenous or exogenous factors that organize chromatin loops in order to promote iPSC induction.

**Scientific Abstract:**

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